GENOMIC-BASED NURSING CARE FOR WOMEN WITH TURNER SYNDROME: GENOMIC-BASED NURSING CARE

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Biologic and technologic advances generated from The Human Genome Project are having a dramatic impact on the expanding role of nurses in current health care practice. New genetic research needs to be transformed rapidly into clinical protocols with recommendations for delivering care to targeted populations. Nurses can contribute significantly, as part of an interdisciplinary approach, to translate genome-based knowledge into benefits for health care and society. In this context, we describe a clinical-genetic investigation protocol, as well nursing diagnosis, interventions and outcomes for clients with Turner Syndrome (TS) at risk for develop gonadal tumors, due the presence of a normal or abnormal Y chromosome.

DESCRIPTORS: genetics; nursing diagnosis; nursing care; genetic counseling; Turner Syndrome

ATENCIÓN DE ENFERMERÍA BASADA EN GENÓMICA PARA LAS MUJERES CON SÍNDROME DE TURNER

Los avances biológicos y tecnológicos generados a partir del Proyecto Genoma Humano están teniendo un impacto dramático en el extenso papel de las enfermeras en la práctica actual del cuidado de la salud. Nuevas investigaciones genéticas necesitan ser transformadas rápidamente en protocolos clínicos con recomendaciones para suministrar cuidados a las poblaciones necesitadas. Las enfermeras pueden contribuir significantemente, como parte de un acercamiento interdisciplinario, traduciendo conocimientos basados en el genoma en ventajas para el cuidado de la salud y la sociedad. En este contexto, describimos un protocolo de investigación clínico-genético e también diagnósticos de enfermería, intervenciones y resultados para clientes con Síndrome de Turner (TS) y riesgo de desarrollar tumores gonadales, debido a la presencia de un cromosoma Y normal o anormal.

DESCRIPTORES: genética; diagnóstico de enfermería; atención de enfermería; consejo genético; Síndrome de Turner

CUIDADO DE ENFERMAGEM BASEADO EM GENÔMICA PARA MULHERES COM SÍNDROME DE TURNER

Os avanços biológicos e tecnológicos gerados a partir do Projeto Genoma Humano estão tendo um impacto dramático na expansão do papel dos enfermeiros na prática atual do cuidado em saúde. As novas pesquisas genéticas necessitam ser rapidamente transformadas em protocolos clínicos, com recomendações para ministrar cuidados a populações alvo. Enfermeiros podem contribuir significantemente, como parte de uma abordagem interdisciplinar, para traduzir o conhecimento baseado no genoma em benefícios para o cuidado em saúde e para a sociedade. Neste contexto, nós descrevemos um protocolo de investigação clínico-genético, assim como diagnósticos de enfermagem, intervenções e resultados para clientes com Síndrome de Turner (ST) e risco de desenvolver tumores gonadais, devido à presença de um cromossomo Y normal ou anormal.

DESCRITORES: genética; diagnóstico de enfermagem; cuidados de enfermagem; aconselhamento genético; Síndrome de Turner

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NURSES IN THE GENOMIC ERA

With the recent completion of the genome sequence and, thus, the successful conclusion of mapping of the human genome, the first phase of the Human Genome Project (HGP), we stand at the dawn of the genomic era. These advances are revolutionizing our understanding of the pathophysiology of human diseases and health in much greater detail than ever before. Genomic-based approaches and resources are beginning to play a key role in redefining our categorization of disease, by making us focus on the biological pathways that lead to them, and providing new approaches to prevention and therapy[1].

Although much work remains to further our understanding of how the genetic code carries out its varied functions, the effect of the HGP on nursing and health care is profound. Translating new human genome research discoveries into clinical practice is happening every day, and nurses in the genomic era will be challenged to recognize genomic influences on risks for diseases, develop and implement nursing interventions, promote health and wellness, while taking into account the appropriate clinical application of genetic technology. Nurses are at the interface of this translation and will increasingly care for individuals and families who have a genetic condition or a genetic component to their health or disease[1]. Thus, there is currently a growing acknowledgement that genetics is not a peripheral specialty concerned only with rare disorders, and of relevance only to nurses and other health care professionals working within this specialist field. There are major implications for nursing and nurse education, as genetics increasingly permeates all aspects of health care. While few nurses in the foreseeable future will be directly involved with either the science or the techniques of genetics, many are already caring for people receiving some type of care or therapy based on genetics. Now, genetics are affecting nursing indirectly, but possibly in drastic ways and, in the near future, genetics will be among the areas of major importance for nursing[2]. Many nursing researchers have pointed that this is a high demand arena for nursing practice in Brazil[3-5].

All nurses, regardless of their specialty or practice area, have a role in delivering genetic health care and managing genetic information. Understanding how our clients regard themselves in light of genomic health care is just a beginning step for nurses in being able to make a difference, when providing nursing care in the genomic era[4]. Genetic information is defined as any information about a client that identifies heritable contributions to his health, or DNA changes acquired during his lifetime. It can be found in genetics tests results, family history and medical records. It is unique and is distinguished from other medical information because it is considered to be private and linked to a person's identity and sense of self, despite its powerful implications for family members as well[6]. Therefore, this kind of information needs to be transformed rapidly into clinical protocols with recommendations for delivering care to targeted populations, and nurses can contribute significantly, as part of an interdisciplinary approach, to translate genome-based knowledge into benefits for healthcare and society[1,4].

In this context, we describe a clinical-genetic investigation protocol, as well as nursing diagnosis, interventions and outcomes for clients with Turner Syndrome (TS) at risk for develop gonadal tumors, due the presence of a normal or abnormal Y chromosome.

TURNER SYNDROME AND GONADAL TUMORS

Turner syndrome is defined as the combination of short stature, gonadal dysgenesis (streak gonads), typical phenotypic characteristics, and urinary, cardiovascular, and skeletal abnormalities, present in individuals with a female phenotype, affecting 1 in 2500 live female births. In 40-60% of women with TS, the karyotypic anomaly is a monosomy 45, X, but a variety of other chromosome anomalies have been found including mosaicism with a structurally normal or abnormal second sex chromosome[7].

The presence of Y chromosome material in individuals with TS is associated with the development of a tumor called gonadoblastoma, which has considerable malignant potential, with an estimated risk around 25%. In 1987, the existence of the *locus* GBY (Gonadoblastoma *locus* on Y chromosome) was hypothesized, which predisposes the dysgenetic gonads to develop gonadoblastoma. Today, the main candidate gene is a probable oncogene known as *TSPY*. Expression of this gene has been detected in gonadoblastoma tissues. The incidence of Y

chromosome sequences in individuals with TS has been evaluated in several studies, and the introduction of the molecular biology techniques, such as Polymerase Chain Reaction (PCR), has revealed the existence of hidden mosaics not detected at the cytogenetic examination. According to the laboratory methodology used, this frequency varied from 0% to 61%[7].

Currently, it is recommended to perform a prophylactic gonadectomy in women with Y chromosome material. However, recent epidemiological studies have questioned the postulated high incidence of gonadoblastoma in these cases[7].

The increasing interest in TS over the past two decades has been motivated by the endeavor to provide life-long support to the clients through multidisciplinary care with quality of life.

CLINICAL-GENETIC INVESTIGATION PROTOCOL

The Multidisciplinary Sex Determination and Differentiation Outpatient Clinic at the Clinical Hospital of the of Ribeirão Preto School of Medicine - University of São Paulo, a tertiary care center, receives many women with TS. The clinical-genetic investigation protocol for these cases starts with the clinical diagnosis of TS, during genetic counseling sessions, provided by a multidisciplinary team composed by physicians, geneticist nurse, psychologist and a social worker, using a face-to-face communication process to present information in the manner that best suits each person needs. The written informed consent for test is obtained from all individuals or their tutors, as an important phase of the pretest education and counseling. Verification of the individual understanding of genetics contents is assessed verbal and periodically during the subsequent counseling sessions.

When a subject presents chromosomal structural alterations or hidden mosaicism, the use of conventional cytogenetic techniques can be ineffective, so that molecular investigation is indicated. In this case, DNA is extracted from peripheral blood leucocytes using standard methods, and screened for the existence of Y chromosome material through PCR, using four different gene sequences spanning the entire chromosome: *SRY* (*Sex-determining Region of the Y*, located on Yp - short arm), *AMGY* and *TSPY* (located on pericentomeric region), and *DAZ* (*Deleted in Azoospermia*, located on Yq - long arm)[8] (Figure 1).

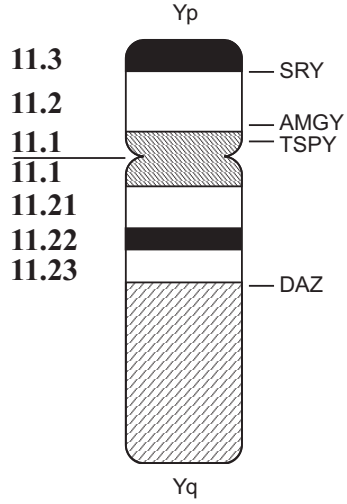

Figure 1 - Schematic representation of Y chromosome showing gene sequences studied by PCR[8]

The pathogenesis of gonadoblastoma and its malignant potential is still rather obscure, but women with TS, dysgenetic gonads and Y chromosome material are at risk for this tumor. This risk has previously been estimated to be almost 30%, and it is directly proportional to age, being significantly higher after puberty due to a lower degree of virilization of the external genitalia and to the intra-abdominal localization of the gonad[7]. Gonadectomy is generally recommended; however, this consensus is questioned by some recent studies. They showed a risk of 7–10% for the development of gonadoblastoma, lower than the previously reported figures, but it may still be unacceptably high in many situations, and parents may still prefer prophylactic gonadectomy. Detailed ultrasound examination of the gonads at regular intervals, or even a magnetic resonance imaging, may be sufficient to monitor some Turner cases with Y chromosome material, especially in cases where clients don't want to have a surgery. Therefore, gonadectomy is still the procedure of choice if one wants to exclude malignancy with absolute certainty[9].

Considering the relationship between gonadoblastoma and the possibility of establishing the X or Y origin of chromosomal fragments in individuals with TS, the team uses the following approach for cases with female or ambiguous genitalia, divided in two groups according their karyotypes: (Group I) Individuals with chromosome mosaicism - A) 45,X/ 46,XX (normal or anomalous X) are followed clinically;

B) 45,X/46,XY (normal or anomalous Y) are informed about the risk of gonadal neoplasm and the need for surgery, which can be performed at the time of diagnosis. In this case, after surgery, they are submitted to the same clinical treatment as the individuals with 45,X/46,XX. (Group II) Subjects with 45,X with mosaicisms are monitored by ultrasound at six month or one year intervals and, in some cases, with magnetic resonance imaging, to detect possible gonadal neoplasm not predicted by cytogenetic and molecular analysis. In cases with 45,X karyotype without mosaicism, we collect cheek cells and urine in order to do a more sensitive PCR to study TSPY sequences[9].

IMPLICATIONS FOR GENOMIC-BASED NURSING PRACTICE

We report some aspects of a geneticist nurse practice as a member of a Brazilian multidisciplinary clinical and research team, carrying out the genetic counseling process and genetic testing, using molecular biology techniques for individuals with Turner Syndrome at risk for gonadal tumors[8].

Genetic counseling has appeared in nursing literature since the early 1960, when nurses' psychosocial support and case-finding responsibilities were emphasized[10]. Genetic counseling became a part of nursing standardized language when it was included in the Nursing Interventions Classification[11], where it is defined as an interactive helping process focusing on assisting an individual, family or group, manifesting or at risk for developing or transmitting a birth defect or genetic condition. Genetic counseling can also be defined as a communication and educational process by which individuals and family members receive information about the nature and limitations of genetic tests, benefits, risks, and meaning of tests results. Included within this process are counseling and support concerning the implications of information gained from genetic tests. Clients must receive adequate information to make an informed decision concerning their health and give informed consent to undergo testing. It is a challenge to present information that is often technically complex and emotionally laden to individuals. Providing individuals with clear, concise, complete and standardized information is essential for informed decision-making. Nurses may receive questions from their clients concerning this process and must be able to address those concerns[1].

The term genetic testing is now used in common vocabulary and with little specificity, often referring to very different applications of testing. However, genetic test is the analysis of human DNA, RNA, chromosomes, proteins, and certain metabolites in order to detect heritable disease-related genotypes, mutations, phenotypes or karyotypes for clinical purposes. Genetic test can yield highly specific information about future risk. Genetic information is improving our understanding about the biology of specific diseases, is increasingly used to more precisely identify at risk individuals, to further characterize diseases, to establish treatment tailored to the genetic profile of the individuals and their diseases[12].

Genetic testing has many benefits in terms of indicating who may benefit from prevention, early intervention and treatment to improve heath. However, there remain many uncertainties, for example the potential for tests results to provoke anxiety, concerns regarding discrimination and social stigmatization. All nurses in preparation for providing genetic services should receive appropriate education that includes foundational information on genetics and genetic health care, as well as knowledge of the implications and complexities of genetic testing, ability to interpret results, and knowledge of the ethical, social and psychological consequences of genetic testing[1].

People with genetic conditions and their families are at risk for many nursing diagnosis for which nurses can apply components of genetic counseling, but not all situations are reflected in the current nursing diagnosis literature, and some diagnoses are still in development stages. In Table 1, we can see some nursing diagnoses for women with TS. When delivering care to individuals with genetic conditions or genetic related concerns, important components of the nursing process are client teaching and counseling interventions that promote the ability of the client to cope with the situation (Table 2), and nursing outcomes. An understanding of diagnoses and outcomes is essential, however, to assist nurses in becoming prepared to use genetic counseling as a nurse intervention. As the role of genetic testing increases in all areas of clinical practice, nurses will need to have a good understanding of what genetic tests are, the indications for their use, skills to support

families throughout the testing process, awareness of the influence of ethnicity, culture, and economics in the client's ability to use genetic information and services. Even nurses without a huge knowledge in genetics can incorporate specific aspects of the genetic counseling process into their clinical practice. The nursing focus is on the identification and prioritization of strategies to promote a desirable outcome for clients manifesting or at risk for developing a genetic condition. According to Williams, nurses use several nursing-sensitive outcomes to monitor the effectiveness of genetic counseling in meeting individuals' psychosocial needs as related to the genetics aspects of their health[10].

Table 1 - Nursing Diagnosis identified during genetic counseling process for individuals with TS and a normal or abnormal Y chromosome and/or their families

Knowledge Deficit - Need to know about TS etiology, day-by-day care, quality of life, prognosis, life expectancy and the purpose of genetic tests and surgery for gonadal tumor prevention.
Social Isolation - Alteration of appearance and feelings about gender identity can lead to social isolation and depression.
Altered Family Process - Experiences of guilt, marital stress, and difficulties in communicating with spouse, children, and extended family.
Decisional Conflict - Decisions about having testing performed are especially controversial when the person who may need test is a child, as well decisions about surveillance and prevention, as prophylactic gonadectomy.
Altered Growth and Development - A decrease in growth velocity occurs as early 18 months of age, but some children present this only when the normal pubertal growth spurt fails to occur. Most people have normal intelligence, and approximately 10% have substantial developmental delays and need special education.

When we are assisting women with TS, we expected that our clients enhance their knowledge about TS and gonadoblastoma risk and are able to participate in health care decisions about the proposed clinical-genetic investigation protocol, as well as to manifest health seeking behavior for available options for surveillance and prevention, such as prophylactic gonadectomy and clinical treatment, accepting health status and also reproductive choices available for individuals with TS. Acceptance of health status relates to the clients' ability to adjust to or come to terms with their genetic health issues. Persons with TS have a feminine gender identity, and lack of X or the presence of a Y chromosome has no relationship to inadequateness as a female, or lack of maternal feelings. When appropriate, it can be explained to the girl that she will be able to marry, enjoy sexual relations, and that other reproductive options such as adoption or receiving an egg donation are available. In the older adolescents and young adults, it is important to reemphasize the potential for a satisfactory life. Indicators of the anxiety control outcome can be used to measure a person's anxiety level, and relief from or exacerbation of anxiety following genetic counseling and testing. The nurse also monitors the individuals' actions directed at managing stressors for coping outcome. Maintaining hope when facing uncertainty or loss is an important outcome of genetic counseling that the nurse can monitor through indicators of the hope outcome[13].

Table 2 - Key components of the genetic nursing intervention for clients with TS and a normal or abnormal Y chromosome

Health Teaching - Providing genetic information regarding the genetics basis of TS and gonadal neoplasm risk in ways that are appropriate to the clients' educational, social, and cultural background. Assessment of factors that influence understanding of genetic information and creation of new ways to present genetic information that overcome barriers that limit clients' abilities to understand and retain genetic counseling information.
Decision Making - Offering reliable information to clients providing them education to help their understanding about the purpose of the genetic test and surgery in order to prevent gonadoblastoma. Participating in ensuring enough information to sign the informed consent term, discussing: benefits, risks and limitations of the genetic test, acknowledgement of the right to refuse testing, health choices, a plan for follow-up care, other available treatment and intervention options, further decision making about surgery necessity upon receipt of test results, as part of the process for genetic testing. Advocating for privacy and confidentiality of genetic test results and information, and practice non discrimination.
Psychological Well-Being - Assessment of adjustment to and coping with genetic information and diagnoses related to TS and gonadoblastoma risk, awareness of individual and/or family knowledge, culture, attitudes, beliefs, and feelings, in meeting client's psychosocial needs. Providing referrals to facilitate them to contact others who have TS through "Portal das Síndromes" (http://www.portaldassindromes.com.br), Magic foundation (http://www.magicfoundation.org) and Turner Syndrome Society of the United States (http://www.turner-syndrome-us.org).

Nurses are at the interface between technology, clinical application of new genetics tests and treatments, and the individuals and families who make use of and are affected by new genetics approaches to health and illness[1]. Therefore, in all practice settings, nurses are starting to participate in the coordination of individual care and collaboration with an interdisciplinary team of health professionals to help clients receive the genetic information and support their needs based on the fourfold responsibilities laid on nurses practice: promoting health, preventing illness, restoring health and alleviating suffering[2]. Nursing professionals' involvement in research related to how individuals and families come to understand their genetic condition, share information within and outside the family and redefine themselves in relationship to new genetic information is needed[1].

In conclusion, because of their unique and holistic approach to care for their clients, nurses have a wealth of knowledge, resources, and research ideas to use in order to further enhance and improve clinical care in the genomic age.

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